REMARKS

Claims 1-50 are pending in the application after entry of this amendment. Claims 1, 3-30, and 32-48, and 50 stand rejected while claim 31 was objected to. Claims 1, 2, 3, 4, 42, 43, 47, and 50 have been amended.

Rejections under 35 USC §102

Claims 1, 6-12, 19-22, 30, 32-35, 42-46, 48, and 50 were rejected under 35 USC §102(b) as being anticipated by US 6,060,246 to **Summerton**. Applicants have amended claim 1 to include the limitations of the original dependent claim 2. Claim 1, as amended, calls for a nucleic binding portion for attracting non-sequence specific binding of nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group. **Summerton** does not identically disclose a nucleic acid binding portion as recited in amended claim 1. The amendment renders the rejection under 35 USC 102 moot and withdrawal of the rejection is respectfully rejected.

Claims 1, 6-7, 9-12, and 19-22 were rejected under 35 USC §102(b) as being anticipated by US 5,900,481 to **Lough**. Claim 1, as amended, calls for a nucleic acid binding portion for attracting and non-sequence specific binding of nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group. **Lough** does not identically disclose a nucleic acid binding portion as recited in amended claim 1. The amendment renders the rejection under 35 USC 102 moot and withdrawal of the rejection is respectfully rejected.

Rejections under 35 USC §103

Claims 2 and 49 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to **Summerton** in view of US 4,935,342 to **Seligson** and further in view of US 5,418,130 to **Platz** or JP2002060671 to **Hatekeyama**. This rejection is traversed.

Applicants have amended claim 1 to include the limitations of the original dependent claim 2. The rejection is believed to now apply to claim 1. The rejection states:

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include the cleavable linkers taught by Summerton in the isolation technique taught by Seligson. As taught by Summerton, "the present invention, by combining rapid capture and concentration of polynucleotides with selective targeting of analyte molecules greatly enhances this process "in contrast to the "generally very slow and inefficient, especially for low-copy sequences" process of conventional hybridization to sequence-specific probes (col. 14, lines 4-15). One of ordinary skill in the art at the time the invention was made would recognize the benefit of enhanced isolation of nucleic acid molecules and would make particular note of the embodiment which incorporates sequence specific capture of nucleic acid molecules in addition to cleavable linkers, which allow for "selective retention on the reagent surface of a target sequence containing polynucleotide" (Col. 8, lines 64-67). The selective retention of target sequences could be amplified on the bead, because "amplification may conveniently be carried out without release of analyte molecule from the rapid pairing reagent, as long as the amplicon region is outside of the target sequence bound to the target specific probe" (col. 14, lines 20-24). One of ordinary skill would recognize the benefit of the cleavable linkers and nucleic acid capture techniques taught and the potential for enrichment of specific target sequences, who would therefore be motivated to incorporate the cleavable linkers and target specific capture molecules into the nucleic acid capture technique taught by Seligson with a reasonable expectation of success (underlining added).

Applicants respectfully request the Examiner to clarify the rejection by identifying which portion of which reference is being modified based on what teaching or motivation in the prior art. The rejection is phrased to indicate that Summerton is the primary reference and is modified by Seligson. Yet as Applicants read the Examiner's proposed combination and modification, Seligson would be modified to include a cleavable linker connected to a target specific probe (using base pairing binding) for "enhancement of specific target sequence." Even if there is motivation in the prior art to so modify Seligson (which Applicants deny), the result of the

proposed modification would not produce a method of isolating a nucleic acid using a solid phase comprising a nucleic acid binding portion for attracting and non-sequence specific binding of nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group, as call for in amended claim 1. Applicants maintain that no *prima facie* case of obviousness has been established and respectfully request withdrawal of the rejection.

The rejection of previous claim 49, may also apply to claim 48 because of the amendment of claim 1. To the extent that it is still relevant therefore, the basis for the rejection is traversed for each of the reasons stated in connection with the rejection of claim 1. Additionally, the examiner states that the '246 patent teaches, at column 14, releasing the nucleic acid from the solid phase into a solution and using this solution in a downstream amplification. In fact, the patent does not teach this but, rather, teaches amplifying the remaining bound nucleic acid that is still immobilized on the solid phase. Only the sequence-specifically bound nucleic acid is amplified. Applicants maintain that no *prima facie* case of obviousness has been established and respectfully request withdrawal of the rejection.

Claims 3-5 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to Summerton in view of US 4,935,342 to Seligson and further in view of US 5,418,130 to Platz or JP2002060671 to Hatekeyama. This rejection is traversed. Again, applicants respectfully request the Examiner to clarify the rejection by identifying which portion of which reference is being modified based on what teaching or motivation in the prior art. The rejection is phrased to indicate that Summerton is the primary reference and is modified by Seligson. Yet as Applicants read the Examiner's proposed combination and modification, Seligson would be modified to include a cleavable linker connected to a target specific probe

(using base pairing binding) for "enhancement of specific target sequence." Even if there is motivation in the prior art to so modify Seligson (which Applicants deny), the result of the proposed modification would not produce a method of isolating a nucleic acid using a solid phase comprising a nucleic acid binding portion for attracting and non-sequence specific binding of nucleic acids and wherein the nucleic acid binding portion includes a ternary or quaternary onium group, as recited in amended claim 1. The Examiner further takes the view that Platz teaches embodiments of claims 3-5 of the present application by virtue of the disclosure of a quaternary ammonium or phosphonium group in a psoralen-based photosensitizing anti-viral compound. This position is wholly unwarranted and unsupportable. Platz does not in fact teach any embodiments of present claims 3-5. Platz provides no motivation for combining the quaternary ammonium or phosphonium groups with the binding materials of Seligson. The field of photosensitized viral inactivation is remote from the present invention. The further reasoning offered by the Examiner that quaternary onium groups "can impart water solubility to the sensitizer molecule" also provides no motivation to adapt these groups to the compounds of the present invention. Increased water solubility is irrelevant and of no value in a solid supported material. Nor would it be of obvious benefit as part of the cleaved fragment of the present binding materials after use. If anything, a less soluble cleaved fragment might facilitate its removal from the isolated nucleic acids.

With respect to the Hatakeyama reference, the rejection states:

The benefit of improved affinity for nucleic acids to a particular solid phase would be obvious to one of ordinary skill in the art who would be therefore be motivated to include a phosphonium or sulfonium group where quaternary ammonium groups have been used in the past with a reasonable expectation of success.

Applicants respectfully request the Examiner to point out with particularity (page and line numbers) identifying where Hatakeyama discloses improved affinity (of phosphonium or

sulfonium groups) for nucleic acids to a particular solid phase. Applicants maintain that Hatakeyama does not disclose such. Furthermore, the rejection does not identify where quaternary ammonium groups have been used with cleavable linkers in the past. Applicants also respectfully direct the Examiner's attention to the request for a non-machine translation of Hatakeyama below. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claim 47 was rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to **Summerton** in view of US 4,935,342 to **Seligson** and further in view of US 5,418,130 to **Platz** or JP2002060671 to **Hatekeyama**. This rejection is traversed for the same reasons explained in the previous paragraph relating to the rejection of claims 3-5. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claims 13-15 and 23-29 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to **Summerton** in view of US 5,707,559 to **Schaap**. This rejection is traversed. Claims 13-15 and 23-29, as presently amended, relates to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization. The rationale outlined in paragraph 10 of the Office Action for combining the teachings of Summerton and Schaap would not produce a nucleic acid binding portion for attracting and non-sequence specific binding of nucleic acids and further would not produce a nucleic acid binding solid phase wherein the nucleic acid binding portion includes a ternary or quaternary onium group, as call for in amended claim 1.

Applicants dispute that a *prima facie* case of obviousness can be made based on combining these two patents. The Examiner alleges that "One of ordinary skill in the art would recognize the benefit of luminescence upon cleavage of a cleavable linker ...". No explanation is given of what the benefit of producing luminescence would be in the context of the present invention, nor can one be found in either reference. Applicants assert that there would be no obvious value in doing so. The Schaap patent provides no motivation for combining its teachings with Summerton. Likewise Summerton does not provide any motivation for employing a chemiluminescent dioxetane as a cleavable linker. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claims 16 and 17 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to Summerton in view of US 6,514,700 to Singh. This rejection is traversed. As stated above, the claims, as presently amended, relate to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization. The rationale outlined in paragraph 11 of the Office Action for combining the teachings of Summerton to provide a method for selective enrichment of particular nucleic acid sequences does not teach or suggest the presently claimed method of isolating nucleic acids regardless of base sequence. Further the combination would not produce a nucleic acid binding solid phase wherein the nucleic acid binding portion includes a ternary or quaternary onium group, as call for in amended claim 1. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claims 36-37 and 41 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to Summerton in view of Mukhamedgaliev and further in view of Reinecke and further in view of US 5,418,130 to Platz or JP2002060671 to Hatekeyama. This rejection is traversed. As stated above, the claims, as presently amended, relate to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization. The rationale outlined in paragraph 12 of the Office Action for combining the teachings of Summerton in view of any of the cited secondary references to provide a method for selective enrichment of particular nucleic acid sequences does not teach or suggest the presently claimed method relating to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization.

It must be pointed out that the **Mukhamedgaliev**, other than the abstract, is in Russian. An English translation is necessary to understand the full teachings of the document in context. .

Applicants respectfully direct the Examiner's attention to the request for an English language translation of Mukhamedgaliev below.

The relevance of the **Platz** patent with regard to the phosphonium group and bromine atom and the alleged suggested advantages is disputed for the same reasons stated above in connection with the rejection of claims 3-5. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Claim 38-40 were rejected under 35 USC § 103(a) as being unpatentable over US 6,060,246 to **Summerton** in view of US 3,855,310 to **Chopdekar** and further in view of US 4,904,819 to **Hagashita**. This rejection is traversed. As stated above, the claims, as presently

amended, relate to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization. The rationale outlined in paragraph 13 of the Office Action for combining the teachings of Summerton in view of either of the cited secondary references to provide a method for selective enrichment of particular nucleic acid sequences does not teach or suggest the presently claimed method relating to the isolation of nucleic acids with a solid phase for binding nucleic acids without distinction among different base sequences and not by a process involving hybridization.

A reference is made to a document by Stern. No such document was cited or provided.

Clarification of this basis for rejection is required or the rejection should be withdrawn. On the assumption that the reference to Stern applies to Chopdekar the rejection is further traversed. The Examiner states:

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teachings in the art of the inclusion of triphenylphosphine containing compounds attached to a resin, as exemplified by Stern [sic] and Hagashita and to incorporate this type of linkage into the nucleic acid isolation technique taught by Summerton.

Neither Chopdekar or Hagashita disclose any triphenylphosphine containing compounds attached to a resin, nor does either reference disclose the use of any triphenylphosphine containing compounds in a Wittig reaction where the phosphorus-containing group would be cleaved from a resin. The further attempted justification:

As taught by Chopdekar, triphenylphosphine groups "find use in a wide variety of processes; the ability of this typical compound to be selectively oxidized to triphenylphosphine oxide permits its use in processes wherein a particular group must be selectively reduced" (col. 1, lines 9-17). The versatility of the triphenylphosphine compound in reductive reactions would be obvious to one of ordinary skill in the art who would therefore be motivated to include the triphenylphosphine group into the solid phase binding of nucleic acids taught by Summerton with a reasonable expectation of success

also fails to provide any motivation for the use of any triphenylphosphine containing compounds in a Wittig reaction where the phosphorus-containing group would be cleaved from a resin or other solid phase. Applicants maintain that no *prima facie* case of obviousness has been established and withdrawal of the rejection is respectfully requested.

Request for Non-Machine Translation of Hatekeyama

In the Office Action of December 12, 2005, numerous claims were rejected in view of a combination of references including Hatekeyama. In the Office Action, paragraph number 7 (page 10), claims 2 and 49 were rejected; in paragraph number 8 (page 12), claims 3-8 were rejected; in paragraph number 9 (page 14), claim 47 was rejected; and in paragraph number 12 (page 20), claims 36-37 and 41 were rejected in view of Hatekeyama et al. Applicants thank the Examiner for kindly providing the machine translation of Hatekeyama et al. However, Applicants maintain that the machine translation is inaccurate, including numerous grammatical and substantive errors. Applicants respectfully request the Examiner to obtain a non-machine translation from a translator in the Translations Branch of the Scientific and Technical Information Center (STIC) in accordance with MPEP 901.05(d) and provide Applicants with a copy of the same. Applicants maintain that serious questions remain regarding what is actually disclosed in Hatekeyama et al. Applicants respectfully request the Examiner to withdraw all rejections based on Hatekeyama et al until the Examiner has obtained an English translation of the reference and provided Applicant with a copy of the same. Applicants maintain that no prima facie case of obviousness has been established with respect to any rejection in view of Hatekeyama et al.

Request for English Translation of Russian Reference

Claims 36-37 and 41 were rejected under 35 U.S.C. 103(a) as being unpatentable over Summerton in view of Mukhamedgaliev et al (1994, Uzbekskii Khimicheskii Zhurnal (6), p. 41-3) and further in view of Reinecke et al (Macromol. Rapid Commun., 1996, vol. 17, No. 15-23) and further in view of Platz et al (U.S. Patent No. 5,418,130; May 1995) or Hatekeyama et al. Applicants note that the rejection relies on Mukhamedgaliev et al, which is in Russian and not English. Applicants maintain that a reference is prior art for all that it teaches. Beckman Instruments v LKB, Produkter A.B., 892 F. 2d 1547, 1551 (Fed. Cir. 1989). It is inappropriate to base a rejection of a patent claim based on only selective portions of a reference ignoring other portions. With respect to reliance on foreign language documents in support of a rejection, MPEP 706.02 states:

... If the document is in a language other than English and the examiner seeks to rely on that document, a translation must be obtained so that the record is clear as to the precise facts the examiner is relying on in support of the rejection. The record must also be clear as to whether the examiner is relying upon the abstract or the full text document in support of a rejection. The rationale for this is several fold. It is not uncommon for the full text document to reveal the document fully anticipates an invention that the abstract renders obvious at best. The converse may also be true, that the full text document will include teachings away from the invention that will preclude an obviousness rejection under 35 U.S.C. 103, when the abstract alone appears to support the rejection. ...

Applicants respectfully request the Examiner to obtain a translation of Mukhamedgaliev et al from the Translations Branch of the Scientific and Technical Information Center (STIC) in accordance with MPEP 901.05(d) and provide Applicants with a copy of the same. Further, Applicants maintain that serious questions remain regarding what is actually disclosed of Mukhamedgaliev et al. According to MPEP 706.02(j), a rejection under 35 U.S.C.

103 should include a recitation of the differences in the claim over the applied references. As such, the Examiner cannot discharge her duties without obtaining an English translation of Mukhamedgaliev et al. and identifying the differences between the claims and the reference, and allowing Applicants to respond to such a rejection with the English translation in hand.

Applicants maintain that in the absence of being supplied with a copy of an English translation of Mukhamedgaliev et al, no prima facie case of obviousness has been established, and withdrawal of the rejection is respectfully requested.

All grounds for rejection having been addressed, and to the best of Applicants' knowledge overcome, Notice of Allowance is respectfully requested.

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